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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/559,986	09/11/2006	James McCarthy	112701-667	6606

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EXAMINER	
SWOPE, SHERIDAN	
ART UNIT	PAPER NUMBER
1652	

NOTIFICATION DATE	DELIVERY MODE
02/03/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATENTS@BELLBOYD.COM

Office Action Summary	Application No.	Applicant(s)	
	10/559,986	MCCARTHY ET AL.	
	Examiner	Art Unit	
	SHERIDAN SWOPE	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 November 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-44* is/are pending in the application.

4a) Of the above claim(s) *5-16 and 22-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 17-21* is/are rejected.

7)☒ Claim(s) *18 and 20* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 December 2005* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *0108*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' election with traverse of Invention I(A) in their response of November 19, 2008 is acknowledged. The elected invention is directed to a polynucleotide encoding the polypeptide of SEQ ID NO: 2. Applicants' traversal is based on the following arguments.

(A) Claim 22 of Group IV, drawn to a transgenic plant, is not patentably distinct from Group I; said groups share a special common structural and functional feature. There is no burden in searching both Groups I and IV.

(B) It would unduly limit Applicants' invention to make the election to a single amino acid sequence [SEQ ID NO: 2 or 16]. Moreover, the claimed sequences are related in that they have at least 70% sequence identity to an amino acid sequence of a polypeptide having cysteine proteinase activity. There is no search burden for searching both sequences.

These arguments are not found to be persuasive for the following reasons.

(A) Reply: For unity of invention to exist, there must be a special technical feature linking all claims; unity of invention cannot exist between a subset of claims. There is an examination and search burden for these patentably distinct inventions due to their mutually exclusive characteristics; a cell and a plant have different structures and functions. The inventions require a different field of search (e.g., searching different classes/subclasses or electronic resources, or employing different search queries); and/or the prior art applicable to one invention would not likely be applicable to another invention; and/or the inventions are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

(B) Reply: The reasons the sequences lack unity of invention are explained in the prior action. Searching more that one sequence would be a burden on the Office.

Claims 1-44 are pending. Claims 5-16 and 22-44 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Claims 1-4 and 17-21 are hereby examined.

Priority

The priority date granted for the instant invention is June 20, 2003, the filing date of EPO 03394056.0, which disclosed the elected invention.

Oath-Objections

The Oath is objected to because the change in the spelling of Mohamed Ben Amor's name is not dated. See M.P.E.P. 605.04(a), which states that, any changes made to the Oath/Declaration should be initialed and dated by the Applicants prior to execution. The Office will not consider whether non-initialed and/or non-dated alterations were made before or after signing of the Oath or Declaration but will require a new Oath or Declaration (37 CFR 1.64).

Information Disclosure Statement

Foreign reference EP 1033405, listed in the Information Disclosure Statement filed January 31, 2008 has not been considered because it has not been provided to the Office. If Applicants wish for the reference to be considered, a supplemental Information Disclosure Statement should be submitted and the reference filed. Any subsequent rejection, based on consideration of the supplemental Information Disclosure Statement, will not be considered a new ground for rejection.

Title- Objections

The title is objected to because it is not descriptive of the elected invention, which is a polynucleotide.

Drawings- Objections

The drawings are objected to because there are two sets, both filed on December 8, 2005. It is unclear which set is to be used.

Figures 1A, 3A, and 4A are objected to because the legend thereto describes a lane "MW"; however, no such lane is said figures.

The drawings are objected to because there are two figures labeled "2A".

Figures 5, 6A, 12 are objected to because the data are not visible.

The drawings are objected to because there are two figures labeled "6A".

The figures are objected to for disclosing sequences that are not identified by a sequence identifier number (SEQ ID NO:). The sequence rules embrace all nucleotide sequences with ten or more bases and all amino acid sequences with four or more amino acids. Said sequences must be disclosed in a sequence listing and identified by a specific SEQ ID NO: (MPEP 2421.02). 37 CFR 1.821(d) requires the use of the assigned sequence identifier number in all instances where the description or claims of a patent application discuss sequences, regardless of whether a given sequence is also embedded in the text of the description or claims of an application. Applicant is required to check the disclosure completely and to make corrections to identify all of the sequences disclosed therein by sequence identifier numbers.

Specification-Objections

The specification is objected to for disclosing sequences that are not identified by a sequence identifier number (SEQ ID NO:). The sequence rules embrace all nucleotide sequences with ten or more bases and all amino acid sequences with four or more amino acids. Said sequences must be disclosed in a sequence listing and identified by a specific SEQ ID NO: (MPEP 2421.02). 37 CFR 1.821(d) requires the use of the assigned sequence identifier number in all instances where the description or claims of a patent application discuss sequences, regardless of whether a given sequence is also embedded in the text of the description or claims of an application. Applicant is required to check the disclosure completely and to make corrections to identify all of the sequences disclosed therein by sequence identifier numbers.

Claims-Objections

Claims 18 and 20 are objected to for "non-native recombinant DNA…", which would be better stated as "recombinant DNA…".

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Utility

Claims 1-4 and 17-21 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility. The specification fails to teach a specific and substantial function for the protein set forth by SEQ ID NO: 2, as encoded by SEQ ID NO: 1. The asserted utility for said protein is as a cysteine protease. However, said assertion is not an assertion of a specific and substantial utility because the family of cysteine proteases is a large and variable family of

enzymes with a large number of variable substrates and the potentiality of being involved in many different cellular processes and diseases. The specification provides no experimental evidence that the protein of SEQ ID NO: 2 has cysteine protease activity. Even if the specification provided evidence that, more likely than not, the protein of SEQ ID NO: 2 has cysteine protease activity, which the specification does not, utility as a cysteine protease is not specific and substantial utility because, as explained above, the family of cysteine proteases is a large and variable family of enzymes. The specification fails to teach specific substrates for the polypeptide of SEQ ID NO: 2, specific cellular processes mediated by said polypeptide, or specific diseases caused by or to be treated with said polypeptide or the encoding polynucleotides. Without such knowledge, the skilled artisan would no know how to use the encoded protein. Mere assertion that the protein is a cysteine protease does not provide a specific and substantial utility.

It is acknowledged that the specification asserts that the protein of SEQ ID NO: 2 has 60% homology with GenBank Z99172 (PGPub [0104]). However, said assertion of homology is not an assertion that the protein of SEQ ID NO: 2 has the same activity as GenBank Z99172. Even if said assertion of homology was an assertion of activity, which it is not, said homology would not provide evidence that, more likely than not, the protein of SEQ ID NO: 2 has the cysteine activity of GenBank Z99172 because GenBank Z99172 has not been demonstrated to have a well-established function as a cysteine protease.

Evidence that a recited protein has a specifically asserted activity can be provided by (i) experimental results demonstrating the recited protein has the asserted activity or (ii) evidence that the recited protein is homologous to a protein that is well-established as having the asserted

utility, wherein the recited protein also comprises the domains, motifs, and amino acids required for the asserted activity.

Therefore, Claims 1-4 and 17-21 are rejected under 35 U.S.C. 101 because the claimed invention lacks a substantial and specific patentable utility.

Claims 1-4 and 17-21 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 19 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the following reasons.

For Claims 19 and 20, the phrase "a cell" renders the claim indefinite. It is unclear whether said phrase means "an isolated host cell" and/or "a cell in vivo". The skilled artisan would not know the metes and bounds of the recited invention. Claim 21, as dependent from Claim 20, is indefinite for the same reason. For purposes of examination, it is assumed that "a cell" means "an isolated host cell". It is noted that transforming cells in vivo would be a patentably distinct invention from transforming isolated host cells, due to their mutually exclusive characteristics.

Claim 19 is rendered indefinite for improper antecedent usage; on line 2, the phrase "a cell" should be corrected to "the cell".

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Even if Claims 1-4 and 17-21 were not rejected under 35 U.S.C. 101/112, first paragraph/enablement, for the reasons stated above, the following rejection would be made.

Claims 1-4 and 17-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for any polynucleotide encoding a polypeptide having at least 70% or 85% homology to SEQ ID NO: 2 or any polynucleotide comprising SEQ ID NO: 1 or comprising a sequence encoding SEQ ID NO: 2, wherein the polynucleotide encodes a cysteine protease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In regards to this enablement rejection, the application disclosure and claims are compared per the factors indicated in the decision In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). These factors are considered when determining whether there is sufficient evidence to support a description that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. The factors include but are not limited to: (1) the nature of the invention; (2) the breath of the claims; (3) the predictability or

unpredictability of the art; (4) the amount of direction or guidance presented; (5) the presence or absence of working examples; (6) the quantity of experimentation necessary; (7) the relative skill of those skilled in the art. Each factor is here addressed on the basis of a comparison of the disclosure, the claims, and the state of the prior art in the assessment of undue experimentation.

Claims 1 and 2 are so broad as to encompass any polynucleotide encoding a polypeptide having at least 70% or 85% homology to SEQ ID NO: 2, respectively. Claims 3 and 4 are so broad as to encompass any polynucleotide comprising a sequence encoding SEQ ID NO: 2, wherein the polynucleotide encodes a cysteine protease. It is noted that by use of "comprising" language, Claims 3 and 4 encompass polynucleotides, wherein the activity is not derived from the sequence homologous to SEQ ID NO: 1.

The scope of each of these claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides broadly encompassed by the claim. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims. Furthermore, the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited

in any protein and the results of such modifications are unpredictable (Galye et al, 1993; Whisstock et al, 2003). In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of Claims 1 and 2, which encompasses all polynucleotides encoding a polypeptide having at least 70% or 85% homology to SEQ ID NO: 2, respectively. The specification does not support the broad scope of Claims 3 and 4, which encompasses all polynucleotides comprising a sequence encoding SEQ ID NO: 2, wherein the polynucleotide encodes a cysteine protease. The specification does not support the broad scope of Claims 1-4 because the specification does not establish: (A) regions of the protein structure which may be modified without affecting the desired activity; (B) the general tolerance of the desired activity to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Since Claims 17-21 further recite vectors, host cells and methods of expressing the nucleic acids of Claim 1, Claims 17-21 are also rejected under 35 U.S.C. 112 first paragraph due to lack of enablement for the same reasons discussed above.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of polynucleotides with an enormous number of amino acid modifications of the polynucleotide of SEQ ID NO: 1. The scope of the claims must

bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of the identity of sequences having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Written Description

Claims 1-4 and 17-21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of polynucleotides molecules encoding a protein with cysteine protease activity. The specification teaches no such polynucleotides. Moreover, the specification fails to describe any representative species by any identifying characteristics or properties other than the functionality of encoding a cysteine protease. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Allowable Subject Matter

No claims are allowable.

Final Comments

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants'

remarks, requests for extension of time, and any other distinct papers be submitted on separate pages. It is also requested that the serial number of the application and date of amendment be referenced on every page of the response.

It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SHERIDAN SWOPE/
Primary Examiner, Art Unit 1652